Feasibility of Planned Endoscopic Submucosal Dissection with Snaring for Gastric Adenoma Compared with Standard Endoscopic Submucosal Dissection

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Background/Aims: Planned endoscopic submucosal dissection with snaring (ESD-S) is thought to shorten operating time spent on submucosal dissection, but may lead to uncertainty of en bloc resection or to a possible increase in tumor-positive margins. The purpose of the present study is to investigate the feasibility of ESD-S as a planned procedure for gastric adenoma.

Materials and Methods: The medical records of 99 patients who underwent ESD-S or ESD for gastric adenoma between May 2011 and May 2012 were retrospectively reviewed. We analyzed the differences between the ESD-S and the ESD groups, focusing on rates of en bloc resection and pathologic complete resection, mean operation time, and complications.

Results: The mean operation time was significantly lower in the ESD-S group than in the ESD group (19.9±11.2 vs. 33.8±19.9, P=0.012). Cases with an operation time under 30 minutes were more frequent in the ESD-S group (88.9% vs. 48.1%, OR=8.615, 95% CI=2.949∼25.168). There were no significant differences in en bloc resection, histologic complete resection, or complication rates between the two groups.

Conclusions: ESD-S has a time advantage over ESD with a comparable complete resection rate. ESD-S can be considered a planned method for available early gastric adenoma. (Korean J Helicobacter Up Gastrointest Res 2014;14:174-180)

Key Words: Endoscopy; Treatment; Time

INTRODUCTION

A minimally invasive endoscopic treatment, endoscopic mucosal resection (EMR), is officially considered the treatment of choice for gastric adenoma (GA) and early gastric cancer without lymph node metastasis. Endoscopic submucosal dissection (ESD) is a unique procedure that does not rely on snare techniques for dissection of submucosal tissue.1-4 The effectiveness of en bloc resection by ESD for large lesions has been described in several papers.2-7 However, ESD is a highly advanced technique, and special expertise in addition to training under the supervision of experienced hands is preferable. Among the several steps involved in ESD, the most difficult step is considered to be the submucosal dissection.8 If it does not go as planned, active bleeding or perforation could result. Snaring at the half-way point in ESD when en bloc resection may be possible after circumferential mucosal incision and an appropriate amount of submucosal dissection, can be performed as a substitute for completion of the submucosal dissection. Planned endoscopic submucosal dissection with snaring (ESD-S) is thought to decrease the amount of operating time spent on submucosal dissection, but it may lead to uncertainty of the en bloc resection or a possible increase in tumor-positive margins.8

To date, there are few studies that have investigated the feasibility of ESD-S. One retrospective Japanese study evaluated the feasibility of ESD-S in comparison with ESD and demonstrated that the mean operation time was not significantly different between the two groups.8 However, that study focused on ESD-S as a rescue modality rather than a planned method for facilitating submucosal dissection; only 20 out of 45 cases (44.4%) were intended to be ESD-S. Recently, planned ESD-S, limited to GA, has been performed for submucosal dissection in order to decrease operation time at our institution. In the present
study, we aimed to retrospectively analyze differences in the outcomes between patients undergoing ESD-S and those undergoing ESD as a planned procedure in order to determine whether snaring at the final stage is feasible in the mean of complete resection.

**MATERIALS AND METHODS**

1. **Patients and specimens**

   We retrospectively reviewed the medical records of patients who underwent ESD-S or ESD for GA between May 2011 and May 2012 at Gospel Hospital, Kosin University College of Medicine (Busan, Korea). ESD-S was identified by chart and photo review to differentiate it from endoscopic mucosal resection after circumferential precutting (EMR-P). ESD-S was defined as the procedure in which half of the submucosa (usually two-thirds), was dissected by knives followed by electrocoagulation snaring as the final tool to remove the lesion from the stomach (Fig. 1). Lesions in the remnant stomach after subtotal gastrectomy or in the gastric tube after esophagectomy were excluded because the number was small and the specific conditions might affect subsequent analysis. Lesions requiring snare resection for controlling critical situations such as perforation or serious massive bleeding during procedures were excluded. Cases whose medical records were insufficient for retrospective analysis were excluded. All lesions were divided into two groups, the ESD-S group and the ESD group. The two operators were experts, who had performed ESD >150 times each over a period of more than four years. The Ethical Committee of the Kosin University College of Medicine approved the study (12-006).
2. Procedures: ESD and ESD-S

The ESD and ESD-S protocols were as follow. All patients provided written informed consent before treatment. Patients fasted the morning of the operation, which was performed under conscious sedation. Marks were made 5 mm outside the tumor edge with an argon plasma coagulator (PSD-60; Olympus, Tokyo, Japan). Epinephrine (1:100,000 solution in saline) was injected into the submucosal layer around the lesion, and the mucosa were 5 mm outside of the marks. When the saline and epinephrine mixture (1:100,000) alone did not sufficiently elevate the tumor, hyaluronic acid was used. After cutting the mucosa, the lesion was dissected using an Insulation tipped diathermic knife (KD-610L, Olympus) or Flex knife (KD-630L, Olympus). In the ESD group, submucosal dissection was completed using an Insulation-tipped diathermic knife or a Flex knife. In the ESD-S group, submucosal resection was performed using an electrosurgical snare 15 mm (SD-210L-15, Olympus) or 25 mm (SD-210L-25, Olympus) in diameter at the final stage of procedure when at least half of the submucosa had been dissected using the knives. Hot biopsy forceps (FD-1L-1, Olympus) were used for bleeding reduction during the procedure or for the treatment of visible vessels on the mucosal defect after removing the lesion.

3. Variables

Age, sex, tumor location, gross morphology, histology type, depth of invasion, specimen size (the greatest diameter of the specimen), tumor size (the greatest diameter of the lesion on actual measurement), usage of anticoagulant and antiplatelet agents, and comorbidities were evaluated in all patients. We investigated the differences between the ESD-S and the ESD groups with regard to the rate of en bloc resection and pathologic complete resection, mean operation time, and complications in an overall analysis.

4. Histopathologic evaluation

All resected tissue was retrieved using a basket, and the size was measured after retrieval. All specimens were stained with hematoxylin and eosin and were evaluated histologically using low-power and high-power light microscopy. Fragmented specimens were reconstructed in order to evaluate the horizontal and vertical margin involvement. Before fixation, the EMR specimens were mounted on a wax block and stretched gently. This step prevents curling of the specimens’ edges and allows better slicing. After fixation, the specimens were sectioned serially at 2 mm intervals. Histologically complete resection was defined as horizontal and vertical margins free of tumor invasion.

5. Complications

Serious intra-procedural bleeding was defined as bleeding that occurred during the procedure (ESD-S or ESD) that was not controlled by electrocoagulation and necessitated hemoclipping. Post-procedural bleeding was defined as clinically evident bleeding, including melena, hematochezia, and hematemeses, with detectable evidence of bleeding from the mucosal defect by urgent endoscopy performed after the operation. Perforation was diagnosed directly during the procedures or based on the presence of free air on a plain chest film or abdominal computed tomography.

6. Statistical analysis

Statistical analysis was performed using the SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Continuous data are presented as the mean and standard deviation. Categorical data are presented as numbers and percentages. Results were analyzed based on the resection technique (ESD-S and ESD). Categorical variables were compared using the \( \chi^2 \) test and Fisher’s exact test, and continuous variables were compared using Student’s t-test. Statistical significance was set at \( P < 0.05 \).

RESULTS

1. Baseline characteristics

Data were reviewed for 99 patients with 99 GAs who were treated by ESD-S (n=45) or ESD (n=54). Age, sex, tumor location, gross type, depth of invasion, mean specimen size and mean tumor size were not significantly different between the two groups (Table 1).
2. Efficacy of ESD-S compared with standard ESD

The en bloc resection rate was higher in the ESD group than in the ESD-S group, but the difference was not significant (100% vs. 91.1%) (Table 2). Furthermore, the lower rate of en bloc resection did not indicate classical piecemeal resection; only one small piece outside the mark of the specimen resulted in non-en bloc resection in three of four cases (Fig. 2). Complete histologic resection was achieved 93.3% of ESD-S cases and 96.3% of ESD cases; there was no statistical difference. Three cases in ESD-S group and 2 cases in ESD group showed horizontal margin involvement; all cases were revealed to be pure adenomas after post resection. We performed argon plasma coagulation ablation for the involved horizontal margin to remove the remnant adenoma.

The mean operation time was significantly shorter in
Table 3. Complications in ESD-S and ESD Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>ESD-S (n=45)</th>
<th>ESD (n=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall complication</td>
<td>4 (8.9)</td>
<td>4 (7.4)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Serious immediate bleeding</td>
<td>1 (2.2)</td>
<td>2 (3.7)</td>
<td>0.669</td>
</tr>
<tr>
<td>Post-procedural bleeding</td>
<td>3 (6.7)</td>
<td>1 (1.9)</td>
<td>0.323</td>
</tr>
<tr>
<td>Perforation</td>
<td>0 (0)</td>
<td>1 (1.9)</td>
<td>&gt;0.999</td>
</tr>
</tbody>
</table>

Values are presented as n (%).
ESD-S, endoscopic submucosal dissection finished with snaring; ESD, endoscopic submucosal dissection.

the ESD-S group than in the ESD group (19.9±11.2 vs. 33.8±19.9, P=0.012). Cases in which the operation time was <30 minutes were more frequent in the ESD-S group (88.9% vs. 48.1%, OR=8.615, 95% CI=2.949∼25.168).

3. Complications

One serious intra-procedural bleeding occurred in ESD-S group, and two occurred in ESD group: effectively managed endoscopically. More post-procedural bleeding occurred in ESD-S group than ESD group (6.7% vs. 1.9%, P=0.323) (Table 3), and these cases were successfully managed with clipping; no surgical intervention was required. During the procedure, one perforation incidentally occurred and was managed by clipping in the ESD group; submucosal dissection was fully completed using an insulation-tipped diathermic knife after clipping without snaring as a rescue method. There were no significant differences in overall complication rates between the two groups.

DISCUSSION

ESD has significant advantages over other endoscopic treatments with regard to controlling the shape and size of the resected specimen and the high probability of en bloc resection of an entire lesion. However, ESD is sometimes very difficult to perform and an operator must overcome many hurdles during the procedure. The snaring technique is basic and is used in polypectomy or EMR. Although snaring is easily performed and is thought to save time, the disadvantage is uncertainty of en bloc resection. When snaring is applied during the ESD procedure, operators should always consider this disadvantage. This concern discouraged us from performing planned ESD-S in the past. We usually used snaring as a rescue method in serious conditions such as massive bleeding during the operation, perforation during the operation, poor cooperation of the patient, and tumor location prohibitive to ESD. However, as our experience accumulated, we gradually accepted that ESD-S shortens operation time with comparable outcomes to ESD, and we started performing ESD-S for GAs.

There was no statistical difference between the ESD-S and ESD groups with regard to rates of en bloc resection and histologic complete resection, although ESD had a higher en bloc resection rate. Unlike piecemeal resection that is typically caused by simple EMR or EMR-P, the piecemeal resection observed in ESD-S is differentiated into two groups. One group is a typical piecemeal resection and the other (three of four) was composed of one nearly en bloc resected specimen and a tiny specimen from outside the marks (Fig. 2). Nearly one half to two thirds of the submucosal layer was dissected, and the remaining incision line was trimmed for easier snaring in ESD-S, thus the chance of dividing the specimen into large fragments was substantially low. Only when the trimming of the remaining incision line is not sufficient for snaring does a small mucosal piece remain after snaring resection. This observation demonstrates that adequate trimming of the incision line is necessary to achieve en bloc resection in ESD-S.

In our study, ESD-S showed time saving advantages over ESD. A previous study did not find that ESD-S resulted in a shorter operation time compared with standard ESD because snaring resection during ESD was performed as a rescue method in problematic cases. We can assume that snaring as a rescue method means that much time has already passed before the decision to snare is made, so it is inappropriate to analyze the efficacy of ESD-S when cases requiring snaring to resolve serious situations are included. Our study analyzed the efficacy of designed ESD-S compared with standard ESD and proved what we had already empirically accepted. A shorter operation time has several advantages. First, it can decrease the workload of an operator. Long operations result in operator fatigue associated with a decrease in concen-
tration. Second, an increased operation time leads to more patient stress. Most patients in Korea undergo ESD in a semiconscious state, so a longer operation time increases both physical and mental stress. Finally, escalation of the amount of sedatives during a long operation is inevitable, and the dosage limit is often reached. When sedatives reach the maximal accumulative dosage, the operator can become agitated, and the attempt to finish the procedure quickly increases the likelihood of serious accidents.

There was no difference in complication rates between ESD and ESD-S. Although there was no statistical significance, post-procedural bleeding was more frequently observed in ESD-S group. This might be due to inadequate prophylactic coagulation after ESD-S. Non-bleeding visible vessels might not be sufficiently coagulated after snaring resection. The surface of the snaring resection has a relatively well-coagulated appearance in comparison with the surface dissected by knives, so operators may overlook prophylactic hemostatic management. Adding to this, shrunken submucosal tissue with snare resection can be responsible for post-procedural bleeding in ESD-S group. Shrunken submucosa would expand slowly after prophylactic coagulation, and therefore hidden blood vessels can be exposed as time goes by, finally causing post-procedural bleeding.

ESD-S seems to be similar to EMR-P because of the electrocoagulation snaring during procedures. However, an adequate amount of submucosal dissection (at least half) is not achieved in EMR-P. One study showed that en bloc resection was achieved in 77.7% of cases by EMR-P, and the rate of en bloc resection of lesions >2 cm was lower (41.2%). The lower en bloc resection rate of large lesions by EMR-P is due to the fact that the amount of submucosal tissue is too much for a snare to constrict, so piecemeal resection can easily occur. However, there is just a small portion of submucosal tissue that needs to be cut by the snare due to the adequate amount of submucosal dissection. Therefore, there is low chance of piecemeal resection.

In the present study, 10% of forceps biopsy proven adenoma with high grade dysplasia was revealed to be carcinoma after ESD or ESD-S. This proportion was lower than usual situation: in the previous research, about 30% to 40% of adenoma with high grade dysplasia was proved to be carcinoma after ESD. This might be explained by two points. The sample size of this study is so small, and the size of the lesion was small in the present study: 18.2±8.8 mm for ESD-S and 9.6±3.5 mm for ESD. Larger adenomatous lesion tends to harbor carcinomatous area.

There are several limitations in our study. First of all, it was retrospective. Although we strictly selected cases in order to avoid bias, our investigation was based on a review of medical records. Additionally, we had a small sample size. We also limited enrolled cases to those treated by only two experts in order to avoid the effect of the procedure being performed by novice operators. Finally, we were unable to evaluate long-term outcomes. In the future, a large-scale randomized controlled prospective study including many operators should be executed to obtain more generalizable results.

Although there were several limitations, this study proved that ESD-S showed comparable en bloc resection rate and histologic complete resection rate with ESD in GA treatment. Additionally, ESD-S has a shorter operation time than ESD. This time advantage results in less stress on the operators and patients and a decreased amount of sedatives being administered. These factors combine to make ESD-S safer than ESD. Though we need more evidences to prove the efficacy of ESD-S, we carefully suggest ESD-S can be considered as a planned method for the resection of available gastric benign epithelial lesions.

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**REFERENCES**


